REMARKS

Claims 1-2, 4, 7-9, 14-26, 33-45 and 48-56 were pending in the application. Claims 8 and 49-56 have been withdrawn from consideration as being drawn to a non-elected invention. Claim 2 has been canceled and claims 1, 4, 7, 9, 14-15, 24-26, 33 and 45 have been amended. Support for the amendments to the claims may be found throughout the specification and claims as originally filed. *No new matter has been added.*

Accordingly, upon entry of the amendments presented herein, claims 1, 4, 7-9, 14-26, 33-45 and 48-56 will be pending in the application. Amendments to and cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Acknowledgement of the Withdrawal of Previous Rejections

Applicants gratefully acknowledge the withdrawal of the previous rejections of claim 45 under 35 U.S.C. §102(b) over Ruvkun *et al.* and Richardson *et al.*

Claim Objections

Applicants respectfully submit that the objection to claim 45 have been rendered moot by the amendment of the claim to correct the inadvertent typographical errors identified by the Examiner.

Applicants respectfully submit that the objection to claim 48 as being of improper dependent form for failing to limit the subject matter of claim 45 is incorrect. Specifically, claim 45 is directed to a cell-free assay composition. Various embodiments encompassed by the term "cell-free assay composition" include assay compositions containing purified, recombinant or partially purified proteins/components, or may be cell-free extracts (*e.g.,* see page 29, lines 18-19 and page 30, lines 6-14). Accordingly, claim 48 further limits the subject matter of claim 45 by specifying that the cell-free assay composition is a cell-free extract.

Claim Rejections Under 35 U.S.C. 112, Second Paragraph

Claim 33 was rejected as being indefinite on the ground that there is insufficient antecedent basis for the phrase "said insulin signaling pathway," in claim 24 from which claim

33 depends. Accordingly, Applicants respectfully submit that claim 33 has been amended to remove reference to claim 24 thus obviating this rejection.

Claim Rejections Under 35 U.S.C. 112, First Paragraph

Claims 4, 9, 14-26, 33-45 and 48 were rejected for allegedly failing to comply with the written description requirement on the ground that the recitation of the term "a mammalian orthologue" of various *C. elegans* genes encompassed by the claims. Applicants respectfully traverse this rejection.

The molecules of the neurotransmitter and insulin signaling pathways were known to be evolutionarily conserved and mammalian orthologues of the *C. elegans* genes recited in the claims were known in the art as of the filing date of the present application. Specifically, the *C. elegans* genes and the corresponding mammalian orthologues are set forth below:

EGL-30 - mammalian G protein Gαq
EGL-8 - mammalian phospholipase Cβ (PLCβ)
DAF-2 – mammalian IGF-1
AAP-1 – mammalian 3-phosphoinisitide dependent protein kinase (PDPK1)
IRS – mammalian insulin receptor substrate (IRS)
AGE-1 – mammalian phosphatidylinositol 3-kinase
PDK-1 – mammalian phosphoinositide kinase 1 (PDK1)
AKT-1 – mammalian p110 catalytic subunit of PI3K
AKT-2 – mammalian AKT/PKI3
DAF-18- mammalian PTEN
RIC-8 – mammalian synebryn
SNARE complex – mammalian syntaxin, SNAP-25 and synaptobrevin/VAMP
UNC-13 – mammalin Munc13

(See, *e.g.,* pages 11, 16-17, 44-47, 52 and 55 of the application and references cited therein).

Thus, in view of Applicants' disclosure and the knowledge generally available to those skilled in the art at the time the present application was filed, it is respectfully submitted that the claimed invention was fully sufficiently described. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 102(b)

Ruvkun *et al.* (US 2001/0029617)

The rejection of claims 14-22, 24-26, 33-36, 38 and 39 as being anticipated by Ruvkun *et al.* has been maintained. Specifically, the Office Actions states that,

> Ruvkun et al. describe studies of dauer recovery in which the exit from dauer stage is prevented by the muscarinic antagonist, atropine. As explained above, the dauer stage represents a stage in which the nematode has an extended lifespan, thus meeting the limitations of the claims (altered activity of muscarinic receptor resulting in extended lifespan).

and further that,

> Ruvkun et al. teach a method that is a blueprint for assaying agents that promote longevity in a test organism that has altered expression of an insulin signaling pathway molecule ....the cholinergic pathway is continuous with the insulin signaling pathway. (Office Action at page 28).

Solely in the interest of expediting prosecution, independent claims 14, 15 and 24-26 have been amended to specify that the claimed assays are directed to a method of identifying an agent capable of "*extending the mature life phase of an organism.*" Support for this amendment may be found in the specification at page 10, lines 7-10 and in the Examples.

In contrast, Ruvkun et al. teach methods of identifying agents that modulate dauer formation, *i.e.,* a dormant larval phase of *C. elegans*. Ruvken *et al.* do not teach or suggest methods of identifying agents that are useful in extending the lifespan of an adult organism. Nor do they teach methods of identifying inhibitors of the EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13 components of the cholinergic pathway.

In view of the above, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Ruvkun be reconsidered and withdrawn.

Pasricha (Gut 35:1319-1321, 1994)

The rejection of claims 14, 24, 33-34, 36 and 38-39 as being anticipated by Pasricha et al. was maintained. Specifically, the Office Action states that

> because "Pasricha et al. teach administering an agent to an organisms with a cholinergic pathway (which humans have), and they measure the ability of that agent to inhibit the cholinergic pathway. While Pasricha et al. do not explicitly teach monitoring the cholinergic pathway indicators recited in the independent claims, this is inherent to their methods ...because botulinum toxin acts by cleaving the SNARE proteins thus blockading the release of acetylcholine, the teaching of the dependent measures reported by Pasricha et al. can reasonably be interpreted as a measure of the activity of the cholinergic pathway indicators, SNARE complex and muscarinic receptors (Office Action, pages 13-14)

Applicants respectfully traverse this rejection. However, solely in order to expedite prosecution, independent claims 14 and 24, as amended, are directed to methods of monitoring the effect of a test agent on an indicator of the cholinergic pathway selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG and UNC-13 or a mammalian orthologue thereof.

In view of the foregoing, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Pasricha be reconsidered and withdrawn.

Dunant *et al.* (1990 J. Physiol. Paris 84:211-219)

The rejection of claims 14 and 24 as being anticipated by Dunant et al. was maintained on the ground that this reference discloses "methods of administering botulinum toxin... to fish and to cells taken from fish" and that "[b]y measuring electrical activity of the organ, Dunant et al were inherently measuring the activity of SNARE proteins and muscarinic receptors, because the mechanism of action of botulinum toxin requires the ability of the toxin to cleave the SNARE proteins and thus blockade the release of acetylcholine." (Office Action at pages 15-16).

Applicants respectfully request reconsideration and withdrawal of this rejection in view o the amendment of claims 14 and 25, as discussed above.

Richardson et al. (1991 Molecular Pharmacology 40:908-914)

The rejection of claims 45 and 48 as being anticipated by Richardson et al. was also maintained on the ground that this reference teaches cell-free assay compositions "comprising purified muscarinic receptors," "assays to determine binding of ligand to the receptors" and "selecting agents (i.e., antibodies) which inhibit the activity (G-protein signaling) of the receptor." According to the Office Action, the "G proteins discussed in Richardson et al. are the 'mammalian orthologues' of [the]EGL proteins recited in the claims." (Office Action at page32)

Applicants traverse this rejection. Richardson et al. teach an assay for probing the interaction of muscarinic receptors with the GTP- binding protein $G_{0.}$ However, contrary to the assertion set forth in the Office Action the mammalian orthologue of EGL-8 is phospholipase Cβ and the mammalian orthologue of EGL-30 is Gαq.

In view of the foregoing, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Richardson et al. be reconsidered and withdrawn.

Gusovsky et al. (Eur. J. Pharm. 206:309-314, 1991)

Claims 45 and 48 have now be rejected as being anticipated by Gusovsky *et al.* on the ground that this reference teaches a cell free assay in which the amphilic peptides mastoparan and melitten inhibit guanine nucleotide-mediated phosphoinositide breakdown, and thus is encompassed by the subject matter of the claims.

Applicants respectfully traverse this rejection. Gusovsky et al. teach that mastoparan and related peptides inhibited the G protein, GTPγS (see Abstract). Accordingly, Gusovsky et al. do anticipate the presently claimed methods which are directed to of identifying a test agent that affects the activity or expression of EGL-30 (phospholipase Cβ), EGL-8 (Gαq) or RIC-8 (synebryn).

In view of the foregoing, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Gusovsky et al. be reconsidered and withdrawn.

Rejection of Claims Under 35 U.S.C. § 103(a)

Claims 1, 2, 7 and 9

Claims 1, 2, 7 and 9 have been rejected as unpatentable over Ruvkun et al. in view of Gems & Riddle (Genetics 154:1597-1610, 2000). According to the Office Action, Ruvkun et al. teach screening assays for identifying agents that affect DAF-18 and other molecules in the insulin signaling pathway, and further teach that the cholinergic pathway is downstream of the insulin signaling pathway. Gems & Riddle teach mutations in pathway molecules that also extend lifespan.

Applicants respectfully traverse this rejection. As discussed previously, the teachings of the primary reference, Ruvkun *et al.,* are focused on methods of identifying modulators of molecules in the insulin signaling pathway such as a DAF polypeptide, an AGE polypeptide or an AKT polypeptide (paragraphs [0049]-[0054]. The teachings of Ruvkun et al. with respect to molecules in the cholinergic pathway are limited to assays monitoring the ability of muscarinic agonists to induce or inhibit the recovery of DAF mutants from the constitutive dauer state. However, Ruvkun et al. neither teach nor suggest that methods of identifying agents capable of extending the mature life phase an organism by assaying an organism having an altered cholinergic **and** insulin signaling pathway as presently claimed. In fact, Ruvkun et al. teach that

none of the muscarnic agonists and antagonists could induce dauer recovery of daf-2 mutants (paragraph [0411].

The secondary reference, Gems & Riddle, fail to cure the deficiencies of Ruvkun et al. Gems & Riddle disclose single mutations that affect longevity in male *C. elegans*. However, like Ruvkun *et al.,* this reference neither teaches nor suggests assays for identifying agents that affect the length of the adult lifespan in an organism containing altered expression or activity of a molecule in both the cholinergic and insulin signaling pathway.

Accordingly, Applicants respectfully request that the rejection of the claims 1, 2, 7 and 9 under 35 U.S.C. 103(a) be reconsidered and withdrawn.

Claims 20, 23 and 37

Claim 23 was rejected as being unpatentable over Ruvkun et al. on the ground that although this reference does not explicitly disclose carrying out the longevity screening assays in the parasitic nematode *A. canimum,* it does disclose that the biochemical pathways found in *C. elegans* are also present in the nematode *A. caninum.* Claims 20 and 37 were also rejected as being unpatentable over Ruvkun et al. on the ground that it would have been obvious to substitute monitoring cellular localization in the assays for monitoring the effect of muscarinic agonists and antagonists on dauer formation disclosed by Ruvkun et al.

Applicants traverse these rejection. As discussed above, Ruvkun *et al.* neither anticipates nor renders obvious claims 1, 14, 15 or 24-46 from which these claims depend. Accordingly, for the foregoing reasons, reconsideration and withdrawal of the rejection is requested.

CONCLUSION

Applicant believes no additional fees are due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. UMY-035RCE from which the undersigned is authorized to draw.

Dated: August 11, 2009

Respectfully submitted,

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